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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,294	01/26/2006	Blas Frangione	05986/100K560-US1	8280

7278 7590 08/07/2008

DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

EXAMINER	
EMCH, GREGORY S	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
08/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,294	FRANGIONE ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *9,11,12 and 16-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10 and 13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-27* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/17/05; 04/04/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's elections without traverse of Group I, claims 1-15, and of the species apolipoprotein J, in the reply filed on 21 April 2008 is acknowledged.

Claims 9, 11, 12 and 16-27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected subject matter, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 21 April 2008.

Claims 1-8, 10 and 13-15 are under examination in the instant office action.

Information Disclosure Statement

Signed and initialed copies of the IDS papers filed on 17 October 2005 and 04 April 2008 are enclosed in this action.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated

by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7, 14 and 15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 5,948,763. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '763 patent are drawn to a method for reducing the formation of amyloid or amyloid-like deposits involving the abnormal folding into a β-sheet structure of a protein or peptide having a sequence predicted to adopt a β-sheet structure, or for reducing the amount of said protein or peptide which has already formed into a β-sheet structure, comprising: bringing into the presence of

said protein or peptide, either prior to or after the abnormal folding thereof into a β-sheet structure, an effective amount of an inhibiting peptide, which inhibits the folding thereof into a β-sheet structure. The claims of the '763 patent are considered obvious variants of the instant claims because reducing the formation of amyloid or amyloid-like deposits with an inhibitory compound that binds to amyloid-beta (as in the patent) is an example of how the patient suffering from an amyloid disease is treated with a compound which binds amyloid-beta (as in the instant claims).

Claims 1-7, 14 and 15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4-12 of U.S. Patent No. 6,274,615. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '615 patent are drawn to a method for delaying the onset of Alzheimer's Disease in individuals predisposed to Alzheimer's Disease or for treating or delaying the onset of other amyloidosis-related diseases/disorders, comprising administering an effective amount of melatonin to a subject in need thereof to inhibit the formation of fibrils associated with Alzheimer's Disease or to reduce, inhibit or reverse the formation of fibrils or amyloid or amyloid-like deposits associated with amyloidosis-related diseases/disorders other than Alzheimer's Disease. The claims of the '615 patent are considered obvious variants of the instant claims because melatonin is an example of a compound which binds amyloid-beta (as in the instant claims; see e.g. col.12, lines 13-43 of the '615 patent).

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 10 and 13-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a patient suffering from Alzheimer's disease (AD) comprising administration of K_6Aβ1-30-NH_2($E_{18}E_{19}$) or of an antibody or antibody fragment which binds to amyloid-beta, does not reasonably provide enablement for treatment of any patient with any amyloid disease comprising administration of any compound which binds to free amyloid-beta in a body fluid of the patient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

Claims 1-7, 14 and 15 are directed to a method of treating a patient suffering from an amyloid disease comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound which binds to free amyloid-beta in a

body fluid of the patient. Claims 8, 30 and 13 are directed to the same method, but these claims recite examples of the compound to be administered (e.g. the elected species of apolipoprotein J) and amyloid-beta binding fragments thereof and mimetics thereof.

Claims 1-7, 14 and 15 are "single means" claims in that they recite "a compound which binds to free amyloid-beta." The instant fact pattern is similar to that in *In re Hyatt*, 798 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), wherein a single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification at most disclosed only those means known to the inventors. In the instant case, the specification only teaches a few exemplary binding compounds (e.g. Table 1, pp.16-17). When claims depend on a recited property (i.e. ability to bind to free amyloid-beta), a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See also *Fiers v. Sugano*, 984 F.2d 164, 25 USPQ2d 1601 (Fed. Cir. 1993) and MPEP §2164.08(a). However, there are a multitude of other specific compounds that potentially could accomplish the claimed function of binding to free amyloid-beta, and no structural requirement is recited for any of the potential compounds in the instant claims. Therefore, the specification fails to provide enough guidance for one skilled in the art on how to practice the instant method, thereby requiring trial and error experimentation to identify compounds meeting the functional limitations of the claims.

The state of the art indicates that the claimed invention is unpredictable. There is no known cure, treatment or preventative measure for Alzheimer's disease and related diseases, as evidenced by Vickers (Drugs Aging. 2002; 19(7): 487-94) who teaches, "Alzheimer's disease (AD) is the leading cause of age-related dementia and is set to markedly increase in incidence with the gradual aging of the populations in both developed and developing nations. Along with most brain diseases and conditions, there is no effective treatment currently available to reverse, slow down or prevent its course."

The specification teaches prophetic examples of treatment of patients with amyloid disease comprising administration of binding compounds of the invention (pp.23-25). The specification teaches that apolipoprotein E binds to Aβ1-40 and Aβ1-42 *in vitro* (pp.30-35) and teaches administration of K_6Aβ1-30-NH_2($E_{18}E_{19}$) to transgenic mice (the Tg2576 APP mouse model), which resulted in Aβ antibody production, significant improvement in behavioral testing, and significantly lowered plaque burden (pp.35-39). Thus, although Applicants have shown that a peptide that elicits antibodies to Aβ improves cognitive function and lowers plaque burden in a mouse model of AD, Applicants have not shown that direct administration of any of the binding compounds of the invention (e.g. the elected apolipoprotein J) lowers plaque burden in an animal model of AD (an amyloid disease). Furthermore, the transgenic mouse model is specific to AD; therefore, the evidence presented in the specification does not apply to all amyloid disease.

The specification fails to provide sufficient guidance for successfully

therapeutically treating human patients with an amyloid disease and since resolution of the various complications in regards to treating these disorders with a binding compound of the invention is not complete, one of skill in the art would be unable to practice the invention without engaging in undue trial and error experimentation. Additionally, a person skilled in the art would recognize that predicting the efficacy of said compounds in humans in an amyloid disease model as highly problematic (see MPEP §2164.03). Indeed, the art teaches that administration of apolipoprotein J would actually contribute to AD pathology and therefore would not treat the disease. DeMattos et al. (Clusterin promotes amyloid plaque formation and is critical for neuritic toxicity in a mouse model of Alzheimer's disease. Proc Natl Acad Sci U S A. 2002 Aug 6;99(16):10843-8. Epub 2002 Jul 26) teaches that apolipoprotein J (also called clusterin) promotes amyloid plaque formation in the PDAPP transgenic mice (p.10846). Thus, although the specification prophetically considers and discloses general methodologies of using the claimed methods, the disclosure is not considered fully enabling of the claims, since the state of the art teaches that treatment of Alzheimer's disease with any agent, including apolipoprotein J, is highly unpredictable.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The

court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement". The instant specification is not enabling because one cannot follow the guidance presented therein and practice the full scope of the claimed methods without first making a substantial inventive contribution.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

As set forth above, inadequate guidance is presented in the specification to overcome the obstacles in practicing the claimed invention. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. Given the lack of working examples involving treatment of any patient with any amyloid disease (AD or otherwise) comprising administering a binding compound of the invention, it is unpredictable as to which variations, if any, meet the limitations of the claims. Therefore, it would require undue experimentation for one of

skill in the art to practice the claimed invention in its full scope.

Claims 1-8, 10, 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-8, 10, 14 and 15 encompass methods, which specifically require the use of an agent to be administered for treatment of an amyloid disease. The claims do not require that the agent possesses any particular conserved structure or other disclosed distinguishing feature. Even though claims 8 and 10 recite a few exemplary compounds of the invention, these claims still recite "an amyloid-beta-binding fragment thereof" or a "mimetic of said compound or fragment." Thus, the claims encompass a genus of molecules that is defined only by ability to bind to amyloid-beta. However, the instant specification fails to describe the entire genus of compounds encompassed by the claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of desired properties in the form of functional limitations. There is not even identification of

any particular portion of any structure that must be conserved or region that is specifically responsible for the desired function. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the encompassed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the full-length compounds recited in claim 8, e.g. the full-length apolipoprotein J, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicants are reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8, 10 and 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and dependent claims are drawn to a method of treating a patient suffering from an amyloid disease comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound which binds to free amyloid-beta in a body fluid of the patient.

The recitation of "a method of treating a patient suffering from an amyloid disease" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See In re Hirao, 535 F.2d

67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). In the instant case, the body of claim 1 does not depend on the preamble for completeness since it recites "administering to a patient in need of such treatment." Additionally, "such treatment" can refer to administration of the recited compound for any reason, and does not necessarily refer to the "amyloid disease" of the preamble. Thus, the process step is able to stand alone and does not specifically achieve the goal set forth in the preamble and it is unclear what therapeutic effect is desired. It is noted that amending the body of independent claim 1 to "administering to the patient in need of such treatment" or something similar would be remedial.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-7, 10 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/27944 to Schenk (Cite No. BE on Applicants' IDS dated 17 October 2005).

The claims are directed to a method of treating a patient suffering from an amyloid disease comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound which binds to free amyloid-beta in a body fluid of the patient.

The Schenk document teaches methods of treatment of patients suffering from an amyloid disease, including but not limited to AD, via administration of antibodies that bind to amyloid-beta or active fragments thereof (p.3, lines 1-10; p.17, lines 37-38), thus meeting the limitations of claims 1, 2, 5 and 13. The reference teaches that some of the antibodies bind specifically to the dissociated from (or soluble form, which is present in blood) (p.12, lines 28-29; p.15, line 7; p.18, lines 3-4) and teaches systemic, e.g. intravenous, administration (p.25, lines 3-6), thus meeting the limitations of claims 3 and 6. The reference teaches dosages of 0.0001 to 100 mg/kg body weight and teaches daily administration (p.24, lines 21-35), thus meeting the limitations of claim 7. The reference teaches mimetics of the antibody to be administered (p.16, lines 28-33), thus meeting the limitations of claim 10.

Since the reference teaches all the limitations of the claims, claims 1-3, 5-7 and 10 are anticipated by WO 99/27944 to Schenk.

Claim 4 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/27944 to Schenk and as evidenced by Ghiso et al. (Cite No. 2 on Applicants' IDS dated 04 April 2008).

The Schenk reference teaches as set forth above but does not teach the added limitation of claim 4, i.e. "wherein the complex is excreted from the patient." However, this non-active method step is necessarily inherent to the disclosure of the Schenk reference as evidenced by the Ghiso et al. reference. . Applicants are reminded that chemical compounds and their properties are inseparable (In re Papesch, 315 F.2d 381,

137 USPQ 43 (CCPA1963)), as are their processes and yields (In re Von Schickh, 362 F.2d 821, 150 USPQ 300 (CCPA 1966)). The Ghiso et al. reference teaches that Alzheimer's soluble Aβ is excreted daily in the urine (entire document, e.g. abstract). Thus, the treatment methods of administering Aβ antibodies which bind to soluble Aβ disclosed by Schenk are also inherently expected to result in the excretion of the soluble Aβ complexed with the Aβ antibodies, thus meeting the limitations of claim 4.

Since the reference teaches all the limitations of the claim, claim 4 is anticipated by WO 99/27944 to Schenk.

Claims 1-3, 5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,434,170 to Andrulis, Jr.

The claims are directed to a method of treating a patient suffering from an amyloid disease comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound which binds to free amyloid-beta in a body fluid of the patient (elected species of apolipoprotein J). As stated above, the recitation of "a method of treating a patient suffering from an amyloid disease" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481

(CCPA 1951). In the instant case, the body of the claims does not depend on the preamble for completeness since it recites "administering to a patient in need of such treatment." Thus, the process step is able to stand alone and since "a therapeutically effective amount" is not specified, a prior art teaching which discloses the administration of apolipoprotein J for any reason meets the limitations of the claims.

Accordingly, the Andrulis, Jr. patent teaches a method for treating a central nervous system or peripheral nervous system cholinergic deficit state in a mammalian organism in need of such treatment, said method comprising administering to said mammal an amount of thalidomide effective in the treatment of a cholinergic deficit state and for a time sufficient to achieve a suitable blood level to treat said cholinergic deficit state (abstract). The patent teaches that said cholinergic deficit state includes AD (col.1, lines 1-10) and teaches that other therapeutic agents include β-amyloid inhibitors (col.5, lines 19-25). The patent also teaches that apolipoprotein J can be co-administered with thalidomide (col.7, lines 61-63), "which may prevent deposition of beta amyloid into brain tissue." Again, it is noted that "a therapeutically effective amount" is not specified by the claims. Although the instant claims do not recite administration of thalidomide, said claims recite the open language "comprising," which does not exclude additional unrecited elements (see MPEP 2111.03). Thus, the claims read on methods comprising additional elements or method steps, such as administration of thalidomide, as taught by the Andrulis, Jr. patent. Moreover, although the patent does not appreciate the recited "activity" of the claimed compound, (binds to free amyloid-beta in a body fluid of the patient, including blood), this would nonetheless

be an inherent outcome induced by administering apolipoprotein J. Thus, absent evidence to the contrary, the patent inherently teaches this "activity" since it teaches administering apolipoprotein J. Thus, the reference meets the limitations of claims 1-3, and 5. The Andrulis, Jr. patent teaches dosages of 50 mg to 500 mg of the β-amyloid inhibitors (col.7, line 45), thus meeting the limitations of claim 7.

Since the patent teaches all the limitations of the claims, claims 1-3, 5 and 7 are anticipated by U.S. Patent No. 5,434,170 to Andrulis, Jr.

Claim 4 is rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,434,170 to Andrulis, Jr. and as evidenced by Ghiso et al. (Cite No. 2 on Applicants' IDS dated 04 April 2008).

The Andrulis, Jr. patent teaches as set forth above but does not teach the added limitation of claim 4, i.e. "wherein the complex is excreted from the patient." However, this non-active method step is necessarily inherent to the disclosure of the Andrulis, Jr. patent as evidenced by the Ghiso et al. reference. The Ghiso et al. reference teaches that Alzheimer's soluble Aβ is excreted daily in the urine (entire document, e.g. abstract). Thus, the treatment methods of disclosed by Andrulis, Jr. are also inherently expected to result in the excretion of the soluble Aβ complexed with apolipoprotein J, thus meeting the limitations of claim 4.

Since the reference teaches all the limitations of the claim, claim 4 is anticipated by U.S. Patent No. 5,434,170 to Andrulis, Jr.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14 and 15 are under 35 U.S.C. 103(a) as being unpatentable over WO 99/27944 to Schenk, in view of Carro et al. (citation CS on IDS dated 17 October 2005).

The claims are drawn to a method of treating a patient suffering from an amyloid disease comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound which binds to free amyloid-beta in a body fluid of the patient, wherein the blood-brain-barrier is permeabilized prior to administration of the compound (claim 14) with IGF-I (claim 15).

The Schenk reference teaches as set forth above and also teaches that the therapeutics can be administered in conjunction with agents that increase its passage across the BBB (p.25, lines 19-23), as in claim 14. The reference fails to teach permeabilization of the blood-brain-barrier (BBB) with IGF-I. However, upon reading the disclosure of the Schenk document, the skilled artisan would have recognized the desirability of developing improved methods for treating AD. Furthermore, the Carro et al. reference teaches that IGF-I induces clearance of Aβ from the brain in a transgenic mouse of AD (Tg2576; Fig.2 and pp.1392-1393). This effect was assumed to be due to IGF-1 increasing the permeability of the BBB (Figs.3, 4, Table 1 and pp.1394-1395), as in claims 14 and 15.

As evidenced by the prior art, the skilled artisan would have known that IGF-I would be useful in methods of treating AD. Furthermore, it would have been reasonable to predict that IGF-I could be used to enhance the antibody treatment disclosed by Schenk by increasing BBB permeability. Thus, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to improve Schenk's methods of treating amyloid disease by administering IGF-I as taught by Carro et al. to yield predictable results. This is because the artisan has good reason to pursue

the known options within his or her technical grasp to obtain predictable results. Such would amount to combination of known equivalents, as the art demonstrates that both treatments would be useful in methods of treating amyloid disease, such as AD.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

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/G.E./

Gregory S. Emch, Ph.D.
Patent Examiner
Art Unit 1649
31 July 2008

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646